A systematic review on prevention and management of wound infections from cochlear implantation

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Abstract

Objective of review :
Surgical site infections are a recognised complication of cochlear implant (CI) surgery with significant morbidity. Our aim was to search for the optimum prevention and management strategy to deal with this issue.

Type of review : Systematic review

Search strategy :
A systematic literature search was undertaken from the databases of EMBASE, CINAHL, MEDLINE®, Web of Science, Scopus and Cochrane Library according to predefined inclusion and exclusion criteria.

Evaluation method : All relevant titles, abstracts and full text articles were reviewed by two authors who resolved any differences by discussion and consultation with senior authors.

Results :
14 articles were included in our review. The overall quality of evidence was low with the vast majority of the studies being retrospective case series and expert opinions. No randomised-controlled trials were noted. We found consistent reports that intra-operative prophylactic antibiotics should be given to all patients undergoing CI and that the vast majority of CI wound infections had grown *Staphyloccocal spp. or Pseudomonas spp.*

Conclusion :
Our review has not identified any reliable or reproducible strategies to prevent and deal with wound infections after CI. We strongly encourage further research within this field and would suggest that a consensus of opinions from a multidisciplinary panel of experts may be a pragmatic way forward as an effective guide.

Keywords : cochlear implants, surgical wound infection, complications, prevention and control.

Key points

- Surgical site infections are a recognised complication of cochlear implantation
- Incidence rates vary in the literature from 1 - 13%
- Our systematic review identified 14 articles that focused on strategies on preventing and managing a wound infection after cochlear implantation
- The overall quality of evidence was low with most studies being retrospective case series and no level 1 evidence available.
- Due to the difficulties in developing prospective and randomised-controlled studies within the field, we propose a multidisciplinary consensus opinion through a Delphi process.

Introduction

The introduction and expansion of cochlear implantation (CI) technology has revolutionised the management of profound hearing loss worldwide [1]. Despite being a relatively straightforward operation, complications can be disastrous with infection contributing to significant morbidity [2].

These operations are generally classified as clean-contaminated due to the risk of pathogenic translocation through the eustachian tube [3]. Post-operative infections have traditionally been divided into the nature (minor vs major) or timings (early vs

delayed) of infection. Minor infections are cases of simple wound inflammation where conservative outpatient management would suffice and major is when the patient requires hospitalisation, requires further surgery, develops central nervous system complications or requires explanation of the device[4]. Early infections occur within the first 4 weeks after implantation and delayed infections occur after. The overall incidence seems to vary throughout the literature with differences seen in adult and paediatric population, however general figures range between 1 - 13% [5,6].

With the burden of soft tissue infections well documented to both patient and health-care institutions, we were motivated to investigate the best practice management to prevent and deal with such a complication. Our aim was to review the literature in the hope of findings strategies that would reduce the need for major treatment or explantation. It would be very useful to distinguish between wound infections and those arising perhaps from contamination of the receiver-stimulator package, but due to a lack of a standardised definition or distinction in the papers (and indeed in practice it can sometimes be very difficult to tell), we incorporated all infection and inflammation pertaining to the surgical site and surrounding soft tissues as 'wound infection'

Methods

This review was undertaken in line with PRISMA-P 2015 guidelines [7]. A literature search was performed on the engines EMBASE, CINAHL, MEDLINE®, Web of Science, Scopus and Cochrane Library using the following medical subject headings (MeSH) and free text words in varying combinations; *cochlear implants, cochlear implantation, auditory implant, auditory prosthesis, Advance Bionics, Cochlear, Oticon, Med-El, wound healing, wound infection, prosthesis-related infections, postoperative complications, bandages, wound heal, wound infect, wound management, wound care, wound complications, wound swell, wound clean, wound dressings, wound stitch, wound suture, wound bandage, anti-infective agents, antibiotic prophylaxis, penicillins, cephalosporins, aminoglycosides, quinolones, clindamycin, metronidazole, trimethoprim, mupirocin, pseudomonic acid, neomycin, fusidic acid, framycetin, polymyxins, chlortetracycline, antisepsis, soaps, iodophors, povidone, iodine, betadine, disinfectant, eusol, dakin, benzalkonium, chlorhexidine, alcohols, hydrogen peroxide, benzoyl peroxide, gentian violet, hypochlorous acid, hexachlorophene, potassium permanganate, silver, silver sulfadiazine, honey* (Appendix 1)

1. Systematic review protocol and data extraction

The initial 15566 results were narrowed down to 9267 titles after duplicates were removed. Two authors (AV and DB) independently screened through the titles and selected 44 abstracts that focused on wound infections after CI. The same two authors subsequently screened the abstracts independently who then reviewed 32 full papers to assess eligibility. All disagreements were resolved by discussion amongst the authors and 14 full text articles were selected that were relevant to our aims.

The excluded papers included case reports, conference proceedings, papers that focused solely on incidence reporting and non-related wound infections. Two full-text articles were unavailable to source and hence were excluded. Studies containing duplicated data from previously published work were also excluded, as were review articles, editorials and letters. No restrictions were placed on study design or study population. (Figure 1)

All titles, abstracts, full text articles and referencing were handled using Mendeley Desktop v1.17 2008-2017. Our selection process is outlined in our PRISMA diagram in Figure 1.

2. Data analysis

Due to the variety of outcome measures employed by different authors, statistical meta-analysis of results was not possible. Results were therefore presented descriptively.

3. Risk of bias and quality assessment

All studies were assessed for quality and risk of bias by both reviewers, according to a modification of the system described in the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0.18 [8]. Because of the large number of retrospective, non-randomized, non-blinded studies, more weight was placed on description of the preventative and treatment methods.

4. Ethical consideration

As the manuscript took the form of a review without the use of patient data or details, ethical review and registration with the local research department was deemed not necessary.

Results

14 full text articles were reviewed looking at evidence-based approach to the prevention and management of wound infections after CI surgery. A summary of the papers and their findings can be found in Table 1. We had broken down the analyses to multiple factors under two main headings; prevention and management.

A. *Prevention of wound infections*

1. Pre-operative factors

There were two published papers, by Clark and Gluth, stating their expert opinion on potentially modifiable factors prior to CI surgery. Clark et al. subjectively felt that swabbing all patients and staff involved in the surgery to identify pathogen like *Staphylococcal species (spp.)* pre-operatively so that they could be treated in adequate time.[9] Suggestions were also made to remove staff from the operating theatre environment if their repeat swabs were still positive. The authors found waxing the patients' hair, having their ears cleaned and skin scrubbed with 0.5% chlorhexidine in 70% alcohol a few days before surgery beneficial for their overall infection risk.[9]

Gluth et al. stated that patient comorbidity was an important risk factor in developing post-op wound infections. They also reviewed the evidence from various

studies with chronic otitis media and recommended that active pathology should first be dealt with before implantation can be considered. This involved surgical approaches of tympanoplasties, mastoid obliterations or blind sac closure and a staged approach after the ear has been rendered disease-free [2]. Both of the aforementioned studies did not provide any hard data to show a reduction in infection rate from the proposed measures.

Low et al.'s retrospective case series found that the only 2 adult CI infections out of 7 in their series of 432 adult and paediatric patients had prior radiotherapy for head and neck tumours and felt that this was a strong contributing factor, due to the impairment in wound healing [10].

2. Antibiotics

i) Type of antibiotics

Hirsch's retrospective case series of 95 patients undergoing CI found that cefazolin was the commonest (83% of cases) pre-operative prophylactic antibiotic used. They reported no major infections and just one minor one of an inflamed incision line in the early post-operative period (within the first month) [11]. This choice of antibiotic was echoed by Almosnino's 2018 series with clindamycin / vancomycin combination used in patients with penicillin allergy [12]. Other studies have reported using cefuroxime and co-amoxiclav [3]. The authors felt these antibiotics would cover the common microorganisms that would migrate from skin or middle ear mucosa and cause an infection.

ii) Time given

Hirsch et al. and Almosnino et al. had the prophylactic antibiotics given 30 minutes before skin incision. Both retrospective non-comparative studies reported no major infections. [11,12]

iii) Duration

Garcia-Valdecasas et al. reported a cohort study on 192 patients who had a combination of ceramic-coated CI (eg. MED-EL implants) and titanium-silicon coated CI (eg. Cochlear Nucleus and Advanced Bionics implants). The authors looked at 4 subgroups of patients and found that patients with titanium-silicon coated implants

who received 6 weeks of clarithromycin post-op in addition to a pre-operative dose of ceftriaxone had significantly lower chances of infections compared to their counterparts who only had the pre-operative ceftriaxone dose (relative risk reduction of 8:1). They hypothesized that the presence of biofilms on these specific implant surfaces played a prime role and that clarithromycin had a bacteriostatic and bacteriocidal properties at low and high doses respectively. Recommended dosing regimen was 125 mg/24 hours in children under 4 years old; 250 mg/ 24 hours in children more than 4 years, and 500 mg/24 hours in adults. Interestingly, the study reported 9 infections, all of which occurred in patients with titanium-silicon coated CI and all of which required explantation despite aggressive intravenous antibiotics and surgical washouts [13].

On the contrary, Basavaraj et al.'s retrospective case series showed that the rate of infection in the early post-operative period was higher in patients who had prolonged prophylactic antibiotics, with infection rates being 5.6% in 5-day regimen and 13% in 7-day regimen [3]. Alongside this, Almosnino reported no difference in infection rates between 2 groups of patients with and without prolonged pre-operative prophylactic antibiotics despite having more diabetics in the group that received only a single shot.[12]

3. Skin prep

Both iodine-based preparations [12] and 0.5% chlorehexidine in 70% alcohol [9] have been reported, although no direct comparisons were made between the two.

4. Incision

There have been recommendations for incisions to be made over a drape to reduce the chance of skin flora migration into the wound [9,12]. Smaller incisions no more than 4cm were cited as the ideal size [2,12] with infection rates reported to be higher in patients who had c-shaped incisions (11.1%) [5] and extended endaural incisions (7.5%). A post-aural approach has been cited to reduce the risk of complications by 15-fold [14]. Gawecki et al. compared long c-shaped and short post-aural incisions when they changed their practice in 2007 and found that although their rates of major skin flap complications halved from 2.43% (11 of 452) to 1.28% (8 out of 624), their results were, however, statistically not significant because of the low

rates of infection [5]. Davids et al. reported similar results where the rates of soft tissue complications were roughly 1% with a smaller incision [6,15].

5. Device preparation

A few papers (non-comparative retrospective series and expert opinion) proposed soaking the electrodes in antibiotic solutions of vancomycin [12] and ampicillin / cloxacillin [9] as well as bathing the mastoid cavity and round window niche with the respective solutions prior to opening the round window membrane.

6. Device placement

Gluth et al. subjectively suggested that the receiver-stimulator package should be placed well away from the incision line and not in contact with patients' spectacles to prevent pressure necrosis.[2] Davids et al. felt that device fixation was an important aspect of paediatric cochlear implantation due to the thinner soft tissue envelope protecting the receiver-stimulator package and relatively more minor head trauma incidences compared to adult patients [16].

7. Closure and sutures

Both Almosnino et al. and Gluth et al. were advocates of multi-layered closure with a tight periosteum layer [2,12]. Clark et al. felt that monofilaments sutures should be used to close the deeper wounds, as they were less likely to form a reservoir for infection compared to braided sutures [9]. Low et al., on the other hand, found that monofilament polyprolene skin sutures were the culprit for 4 out of 5 stitch abscess in paediatric CI patients [10]. Cryanoacrylate adhesives were proposed as a method for skin closure [12].

8. Dressings / wound protection

Almosnino's protocol of mastoid dressings for 24 hours followed by a shower on the first post-operative day did not have any significant impact on rates of wound healing, infection or skin reaction although there were no comparative data available.

B. Management of wound infections

1. Types of bacteria

Staphylococcal spp. and *Pseudomonas spp.* were the commonly identified bacteria in the vast majority of studies [1,5,6,10,14,17,18]. Recognised subtypes of *Staphylococcal spp.* include *aureus* as well as methicillin-resistant and susceptible *epidermidis* strains [17]. Davids et al. had reported that 2 patients in their series of 452 recipients of CI who had suffered trauma and migration of their magnets went on to grow *Haemophilus influenzae* in their swabs [6].

Biofilm production on package complexes has been suggested as one of the main contributing factors in delayed and recurrent wound infections.[1,17] Olsen et al. had visually assessed their infected implants during surgical treatment for biofilms and sent swabs away for microbiological culture and sensitivities. They noted that 8 out of 11 infected implants had biofilm growths of which 7 were ultimately explanted. 5 of these implants cultivated *Staphylococcal aureus* [1]. In Palau et al.'s series, scanning electron microscopes were used to examine the 3 explanted CIs, where 2 were noted to have *Staphylococcal aureus* and *epidermidis* biolfilms on them [17].

Pseudomonas aeruginosa infections were felt to be more sinister and resulted in explantation in 2 out of the 4 serious wound infections in Kabelka et al.'s retrospective series [14]. In agreement with other published data, the authors felt that *Pseudomonal spp.* infections tend to manifest as gradual soft tissue swellings which ultimately results in a 'pseudocapsule' around the implant, denuding the blood supply and hence rendering systemic antimicrobial therapy ineffective. This commonly results in a fistula with surrounding granulation tissue and serous secretions. As such, they recommended that these implants would serve better being explanted straight away rather than persevering with antimicrobial therapy or surgical washouts[14].

2. Antibiotics

Various different antibiotic regimens have been used based on local microbiological guidelines, culture and sensitivity of organisms grown and preference of surgeons.

In Kabelka et al.'s series, they had used a combination of ceftazidime and tazocin for 16 days alongside frequent irrigation with polymixin, neomycin and hydrogen peroxide for one of their infected CI, which unfortunately required explantation after 5 weeks. Another case, which grew *Pseudomonas spp.,* had 21 days of ceftriaxone and ciprofloxacin combination therapy followed by 4 weeks of oral ciprofloxacin before being explanted. They successfully saved two implants, which required drainage of pus and intravenous co-amoxiclav for *Staphloccocal aureus* growth [14].

Davids et al. had 2 cases which grew *Staphloccocal aureus* that were successfully treated with cefazolin (duration not stated) [6]. The 2 cases that grew *Haemophilus influenzae* after trauma initially settled with intravenous Tazocin, however recurred 6 months later requiring explantation.

Olsen et al. had generally treated postoperative infections with beta-lactamase inhibitor antibiotics (eg. Dicillin). This was provided microbiological swabs had not displayed resistance or grown an organism sensitive to another microbial agent. In severe cases, intravenous cephalosporins were used in combination with metronidazole [1].

Palau et al. reported 7 cases of wound infection without device exposure of which 4 cases were successfully treated with oral co-amoxiclav, with swabs growing *Staphlococcal aureus* and methicillin sensitive *Staphylococcal epidermidis.* 2 patients with methicillin-resistant *Staphylococcal epidermidis*, on the other hand, were successfully treated with oral levofloxacin [17].

Although many of the studies had not stated their duration of treatment, Low et al. subjectively felt that a prolonged intravenous administration of at least 6 weeks should be attempted alongside direct topical antibiotics to the device through washouts and irrigation tubes [10].

3. Surgical treatment

i) Washouts

Low et al. were able to salvage their 8 infected CI with a combination of washouts and antibiotics. They performed local debridement of the infected wound and a thorough washout of the device with chlorhexidine and erythromycin. They had occasionally transposed the device to a different pocket if the overlying skin did not appear healthy. Post-operatively, a butterfly needle was left in place to allow daily antibiotics irrigation (based on culture and sensitivities or erythromycin if no growth) for 5 days [10].

In Olsen et al.'s series, they had ensured pus swabs were sent for culture and sensitivities and had used Genta-coll®, a resorbable collagen sponge containing gentamicin, around the implant. They hypothesized that this would help deliver a high concentration of antibiotic substance directly onto the implant, which would help against biofilms. This modality saved 3 out of the 7 wound infections that underwent surgical therapy [1].

ii) Flaps and Repositioning

In an expert consensus document, Rubin and Papsin emphasized that adequate covering of a CI device was vital in reducing the need for explantation. They referred to two separate series' where 8 out of 9 patients with device exposure eventually underwent explantation in comparison to 3 out of 17 wound infections without device exposure [18].

Gawecki et al. strongly advocate a rotational two-flap technique to cover an infected CI alongside intensive targeted antibiotic therapy can be effective and should be first line of treatment. They had employed this philosophy for the delayed major skin flap complications that presented after 1 month and up to 10 years post-implantation. The two layers were described as skin with a subcutaneous layer and muscle with fascia and had been successful in 3 out of 4 of their wound infections.

Rubinstein described four cases were the pedestal of the CI had become exposed through skin infections and were subsequent moved to a healthier site and covered with a combination of pericranial and temporalis muscle flaps with good effect [19].

iii) Explantation

This is ultimately the treatment for patients who have had unsuccessful primary treatment or on-going morbidity from their infection [5].

Discussion

Summary of main results

Our systematic review of the 14 articles found a general lack in high-level evidence on ways of preventing and managing wound infections in CI (Table 1). The vast majority of studies were level 4 retrospective case series based on the Oxford Centre for Evidence-based Medicine grading [20]. The highest quality of evidence was a cohort study by Garcia-Valdecasas et al. [13] conducted in Spain and published in the Laryngoscope in 2009. The lack of randomised-controlled trials and systematic reviews precluded us from conducting a meta-analyses.

Quality of evidence, clinical applicability and potential biases in review

We divided the articles into those focusing on prevention and management of CI wound infections and had 5 and 8 articles in each category respectively (Table 1). Gluth et al.'s expert opinion article published in Cochlear Implants International in 2011[2] was included in both categories, although we also found information on prevention in some of the studies grouped under the management heading.

In the prevention category, Garcia-Valdecases et al.'s comparative cohort study provided some insight into the how wound infections can differ in varying implants due to their surface coating. The comparisons between ceramic and titanium-silicone implants were marred by their unequal numbers in all four arms (21 and 24 patients in ceramic arm vs 76 and 75 in the titanium-silicon arm), however, the authors strongly suggest that patients with titanium-silicone (eg. implants (Cochlear Nucleus and Advanced Bionics) do have fewer wound infections when covered with 6 weeks of post-operative clarithromycin (relative risk 8.1) [13]. The findings may play a role in helping patients decide between their choice of implant type and brand as well as guide clinicians in their consent process for wound infection risks and post-operative management. Interestingly, very few centres cover patients with a long course of post-operative antibiotics, as seen in our review, and none have reported a wound infection rate as high as Garcia-Valdecases et al.'s 10.67% [13]. We were unable to find explanations to account for the outlier number of infections in this series nor the reason the infections only occurred on titanium-silicone implants despite fairly equal baseline characteristics across all four subgroups. One may postulate if there could have been issues with implant batch or sterility over the study period that predisposed to biofilm formation or wound infection'

The choice, duration and regimen of prophylactic antibiotics remain a contention in the literature, although there seems to be a general agreement that all CI patients should receive them due to its role within the early post-operative period (first 30 days) [11]. The lack of comparative studies in Hirsch et al. and Basavaraj et al. series make it difficult to form a consensus opinion especially as their findings of prolonged prophylactic antibiotics show increased infection rates in contradiction to Garcia-Valdecases et al.'s results [3,11,13]. The concordance of antibiotic type used by Hirsch et al. and Almonisno et al. suggests that cefazolin, or perhaps any other 1st

general cephalosporin, may be a suitable prophylaxis agent for *Staphylococcal spp*..[11,12,21] However, its lack of action against *Pseudomonas spp*[21], which is also commonly found in wound infections with a high rate of explantation [14], would suggest that well-conducted comparative trials should be done to investigate newer and broader-spectrum agents against both gram positive and negative microorganisms. (eg. Tazocin, Gentamicin, Co-Amoxiclav).

Another consistent recommendation within the literature was the use of smaller post-aural incisions [2,5,12,14], however the evidence supporting this was generally weak. One comparative study by Gawecki et al. showed that although the rates of skin flap complications had halved with smaller incisions, this was statistically insignificant. It is difficult to power studies with enough numbers in each arm for very low incidences of occurrence, such as infections. It is now common practice that smaller incisions are employed to minimise flap failures and breakdown, however a correlation with wound infection has not been studied. Despite the lack of evidence, common sense would dictate that a smaller incision would provide a lesser raw surface area for microorganisms to grow in, reducing surgical site infection [22,23] while also minimising post-operative pain morbidity. The recommendations for skin prep, device preparation and placement, method of wound closure and post-operative dressings were generally based on single centre experience and thus difficult to support.

Implications for clinical practice

Reviewing the studies that focused on the management of CI wound infections, we found fairly consistent reports that the vast majority of infections were caused by *Staphyloccocal spp.* and *Pseudomonas spp. Pseudomonal spp*. appeared to be the more sinister with a 100% explantation rate, although this was only from 2 patients [14]. Two studies had reported their experience with biofilm formation on the implant surfaces [1,17] which would certainly account for the relapsing infections also seen in our experience. The concept of biofilms on implant surfaces is certainly emerging with growing evidence seen in dental [24] and other titanium implants [25].

Despite the relative certainty in causal microorganisms, the intended therapy seemed to vary amongst the different studies. The evidence behind type and duration of antibiotics as well as nature of surgical treatment was inconsistent and insubstantial mainly due to the overall small numbers and lack of comparisons in treatment methodologies (Table 1). There was, however, a trend of effectiveness of penicillin-based and cephalosporin antibiotics against *Staphyloccoccal spp.*

The management of wound infections with device exposure requires a more aggressive treatment strategy due to the higher risk of explantation[26]. The mostly opinion-based reports we had found suggest that these implants should be treated with antibiotics and surgically covered with flap transposition[5] or moved to a safer location[19] in an attempt to salvage the package. The latter can be difficult to achieve without accidental removal of the electrodes from the cochlear and ought to be performed with threshold monitoring on table. Our own practice, based on accumulated personal experience is that such measures can be fruitful in dry implant exposures, however not in discharging wounds where we find the failure to eradicate infection rate is higher and explanation would be a better first-line option to hasten recovery, although we do not have rigorous data to fully support this.

The lack of separated data makes it difficult to compare prevention and management strategies between adults and children. Most studies [4,13,5] have found the incidence of wound infections to be similar across both subgroups, and generally espouse similar management strategies, although there are some suggestions that device fixation[16] may be more pertinent in children who are liable to the implant package slipping due to their anatomy and daily activities. Low et al.[4] found that stitch abscess was the commonest contributing factor in children mostly from monofilament polyprolene sutures used, although similar risks could easily be postulated to exist amongst adults.

We were also unable to find a clear and consistent methodology across most of the papers (except Hirsch et al.)[11] on how the diagnoses of wound infections were made as well as which member of team had reached them. The lack of a diagnostic

robustness could well have bearings on the suitability and efficacy of management strategy employed especially if they were to be replicated for patients with post-implantation complications.

Implications for research

Looking forward, we feel that the paucity in evidence represents a void in this important aspect of post-operative CI care. We appreciate that conducting large scale randomised-controlled or comparative trials may not be a feasible way to answer the questions we set out to discover in this review. A more pragmatic alternative may be a consensus opinion from a multidisciplinary panel of experts comprising of surgeons, audiologists and microbiologists through a Delphi process to streamline pre-operative management and post-operative treatment strategies. Additionally, the creation of a national database of implants, similar to the National Joint Registries [27], would amass a large collection of data that could yield pertinent information on how such infections are treated at various implant centres across the country with the aim of reducing unwanted variation based on successful techniques. We also appreciate that implantation in ENT is a relatively new and growing field and can draw lessons from specialties such as orthopaedics that have acquired an abundance of experience and research data on infection prevention and management with implants. Lastly, we suggest that future laboratory endeavours should focus on identifying biofilm formation on the varying implant surfaces to identify prevention strategies as well as to guide clinicians and patients in their choice of implants.

Conclusion

The evidence behind prevention and management techniques for CI-related wound infections is lacking. Because of this, we are unable to form a consensus or recommendations to guide other implant units on the optimum method of treatment

and strategies to reduce explantation rates. Further research in this area is highly desirable, perhaps through multi-centre data and randomised trials, especially as these infections present a substantial morbidity to the patient while incurring large financial costs to healthcare institutions.

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Appendix 1. Search strategy

Medline

1. Cochlear Implants/ or Cochlear Implantation/
2. (auditory adj5 (implant* or prosthe*)).mp
3. (Advance bionics or Cochlea* or Oticon or Med-El).mp
4. 1 or 2 or 3
5. Wound Healing/ or exp Wound Infection/ or Prosthesis-Related Infections/ or exp postoperative complications/ or exp Bandages/
6. (wound* adj5 (heal* or infect* or management or care or complication* or swell* or clean* or dressing* or stitch* or suture* or bandage*)).mp
7. (exp Anti-Infective Agents/ or Antibiotic Prophylaxis/ or exp Penicillins/ or exp Cephalosporins/ or exp Aminoglycosides/ or exp Quinolones/ or exp Clindamycin/ or exp Metronidazole/ or exp Trimethoprim/ or exp Mupirocin/ or exp Neomycin/ or exp Fusidic Acid/ or exp Framycetin/ or exp Polymyxins/ or exp Chlortetracycline/)
8. (antibiotic* or antimicrobial* or antibacterial* or penicillin* or cephalosporin* or aminoglycoside* or quinolone* or clindamycin or metronidazole or trimethoprim or mupirocin or pseudomonic acid or neomycin or fusidic acid or framycetin or polymyxin* or chlortetracycline)
9. (exp antisepsis/ or exp Soaps/ or exp Iodophors/ or exp Chlorhexidine/ or exp Alcohols/ or exp Hydrogen Peroxide/ or exp Benzoyl Peroxide/ or exp Gentian Violet/ or exp Hypochlorous Acid/ or exp Hexachlorophene/ or exp Potassium Permanganate/ or exp Silver/ or exp Silver Sulfadiazine/ or exp Honey/
10. (antiseptic* or soap* or iodophor* or povidone or iodine or chlorhexidine or betadine or alcohol* or disinfectant* or hydrogen peroxide or benzoyl peroxide or gentian violet or hypochlorit* or eusol or dakin* or hexachlorophene or benzalkonium or potassium permanganate or silver or silver sulphadiazine or honey*)
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 and 11

Embase

1. exp cochlea prosthesis/ or cochlear implantation/
2. (auditory adj5 (implant* or prosthe*))
3. (Advance bionics or Cochlea* or Oticon or Med-El)
4. 1 or 2 or 3
5. exp wound healing/ or wound infection/ or infection/ or exp postoperative complication/ or exp bandage/
6. (wound* adj5 (heal* or infect* or management or care or complication* or swell* or clean* or dressing* or stitch* or suture* or bandage*))
7. exp antiinfective agent/ or exp penicillin derivative/ or exp cephalosporin derivative/ or exp aminoglycoside/ or exp quinolone derivative/ or exp clindamycin/ or exp metronidazole/ or exp

trimethoprim/ or exp pseudomonic acid/ or exp neomycin/ or exp fusidic acid/ or exp framycetin/ or exp polymyxin/ or exp chlortetracycline/

8. (antibiotic* or antimicrobial* or antibacterial* or penicillin* or cephalosporin* or aminoglycoside* or quinolone* or clindamycin or metronidazole or trimethoprim or mupirocin or pseudomonic acid or neomycin or fusidic acid or framycetin or polymyxin* or chlortetracycline)
9. exp antisepsis/ or Soaps/ or exp iodophor/ or exp chlorhexidine/ or exp alcohol derivative/ or exp hydrogen peroxide/ or exp benzoyl peroxide/ or exp crystal violet/ or exp hypochlorous acid/ or exp hexachlorophene/ or exp permanganate potassium/ or exp silver/ or exp sulfadiazine silver/ or exp honey/
10. (antiseptic* or soap* or iodophor* or povidone or iodine or chlorhexidine or betadine or alcohol* or disinfectant* or hydrogen peroxide or benzoyl peroxide or gentian violet or hypochlorit* or eusol or dakin* or hexachlorophene or benzalkonium or potassium permanganate or silver or silver sulphadiazine or honey*)
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 and 11

Cinahl

1. (MH "Cochlear Implant")
2. (auditory adj5 (implant* or prosthe*))
3. ("Advance bionics" or Cochlea* or Oticon or Med-El)
4. S1 OR S2 OR S3
5. (MH "Wound Healing") or (MH "Wound Infection+") or (MH "Prosthesis-Related Infections") or (MH "Postoperative Complications") or (MH "Bandages and Dressings+")
6. (wound* N5 (heal* or infect* or management or care or complication* or swell* or clean* or dressing* or stitch* or suture* or bandage*))
7. (MH "Chlorthalidone") or (MH "Polymyxins+") or (MH "Fusidic Acid") or (MH "Neomycin") or (MH "Mupirocin") or (MH "Trimethoprim+") or (MH "Metronidazole") or (MH "Clindamycin") or (MH "Antiinfective Agents, Quinolone+") or (MH "Aminoglycosides+") or (MH "Cephalosporins+") or (MH "Penicillins+") or (MH "Antiinfective Agents+")
8. (antibiotic* or antimicrobial* or antibacterial* or penicillin* or cephalosporin* or aminoglycoside* or quinolone* or clindamycin or metronidazole or trimethoprim or mupirocin or pseudomonic acid or neomycin or fusidic acid or framycetin or polymyxin* or chlortetracycline)
9. (MH "Honey") or (MH "Silver Sulfadiazine") or (MH "Silver") or (MH "Hexachlorophene") or (MH "Hypochlorous Acid+") or (MH "Gentian Violet") or (MH "Peroxides+") or (MH "Hydrogen Peroxide") or (MH "Alcohols+") or (MH "Chlorhexidine") or (MH "Iodophors+") or (MH "Soaps") or (MH "Antiinfective Agents, Local+")

10. (antiseptic* or soap* or iodophor* or povidone or iodine or chlorhexidine or betadine or alcohol* or disinfectant* or hydrogen peroxide or benzoyl peroxide or gentian violet or hypochlorit* or eusol or dakin* or hexachlorophene or benzalkonium or potassium permanganate or silver sulfadiazine or silver sulphadiazine or honey*)
11. S5 OR S6 OR S7 OR S8 OR S9 OR S10
12. S4 AND S11

Web of Science

1. (auditory NEAR/5 (implant* or prosthe*))
2. ("Advance bionics" or Cochlea* or Oticon or Med-El)
3. #2 OR #1
4. (wound* NEAR/5 (heal* or infect* or management or care or complication* or swell* or clean* or dressing* or stitch* or suture* or bandage*))
5. ((antibiotic* or antimicrobial* or antibacterial* or penicillin* or cephalosporin* or aminoglycoside* or quinolone* or clindamycin or metronidazole or trimethoprim or mupirocin or "pseudomonic acid" or neomycin or "fusidic acid" or framycetin or polymyxin* or chlortetracycline))
6. ((antiseptic* or soap* or iodophor* or povidone or iodine or chlorhexidine or betadine or alcohol* or disinfectant* or "hydrogen peroxide" or "benzoyl peroxide" or "gentian violet" or hypochlorit* or eusol or dakin* or hexachlorophene or benzalkonium or "potassium permanganate" or silver or "silver sulphadiazine" or honey*))
7. #6 OR #5 OR #4
8. #7 AND #3

Scopus

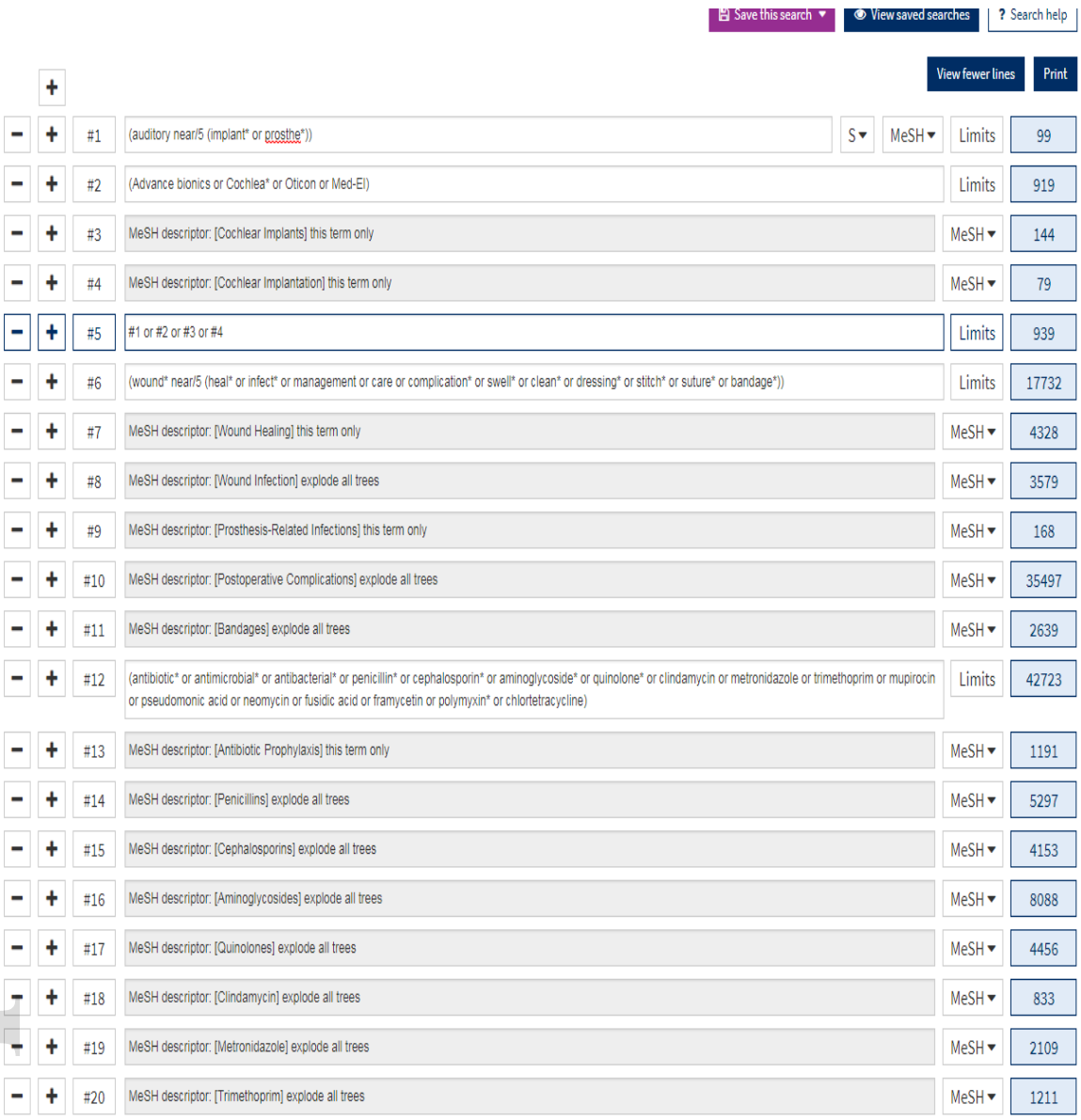
1. TITLE-ABS-KEY ((auditory W/5 (implant* OR prosthe*)))
2. TITLE-ABS-KEY (("Advance bionics" OR cochlea* OR oticon OR med-el))
3. (TITLE-ABS-KEY ((auditory W/5 (implant* OR prosthe*)))) OR (TITLE-ABS-KEY (("Advance bionics" OR cochlea* OR oticon OR med-el)))
4. TITLE-ABS-KEY ((wound* W/5 (heal* OR infect* OR management OR care OR complication* OR swell* OR clean* OR dressing* OR stitch* OR suture* OR bandage*)))
5. (TITLE-ABS-KEY (antibiotic* OR antimicrobial* OR antibacterial* OR penicillin* OR cephalosporin* OR aminoglycoside* OR quinolone* OR clindamycin OR metronidazole OR trimet

hoprim OR mupirocin OR "pseudomonic acid" OR neomycin OR "fusidic acid" OR framycetin) OR TITLE-ABS-KEY (polymyxin* OR chlortetracycline))

6. (TITLE-ABS-KEY (antiseptic* OR soap* OR iodophor* OR povidone OR iodine OR chlorhexidine OR betadine OR alcohol* OR disinfectant* OR "hydrogen peroxide" OR "benzoyl peroxide" OR "gentian violet" OR hypochlorit*) OR TITLE-ABS-KEY (eusol OR dakin* OR hexachlorophene OR benzalkonium OR "potassium permanganate" OR silver OR "silver sulphadiazine" OR honey*))
7. (TITLE-ABS-KEY ((wound* W/5 (heal* OR infect* OR management OR care OR complication* OR swell* OR clean* OR dressing* OR stitch* OR suture* OR bandage*)))) OR ((TITLE-ABS-KEY (antibiotic* OR antimicrobial* OR antibacterial* OR penicillin* OR cephalosporin* OR aminoglycoside* OR quinolone* OR clindamycin OR metronidazole OR trimethoprim OR mupirocin OR "pseudomonic acid" OR neomycin OR "fusidic acid" OR framycetin) OR TITLE-ABS-KEY (polymyxin* OR chlortetracycline))) OR ((TITLE-ABS-KEY (antiseptic* OR soap* OR iodophor* OR povidone OR iodine OR chlorhexidine OR betadine OR alcohol* OR disinfectant* OR "hydrogen peroxide" OR "benzoyl peroxide" OR "gentian violet" OR hypochlorit*) OR TITLE-ABS-KEY (eusol OR dakin* OR hexachlorophene OR benzalkonium OR "potassium permanganate" OR silver OR "silver sulphadiazine" OR honey*)))
8. ((TITLE-ABS-KEY ((auditory W/5 (implant* OR prosthe*)))) OR (TITLE-ABS-KEY (("Advance bionics" OR cochlea* OR oticon OR med-el)))) AND ((TITLE-ABS-KEY ((wound* W/5 (heal* OR infect* OR management OR care OR complication* OR swell* OR clean* OR dressing* OR stitch* OR suture* OR bandage*)))) OR ((TITLE-ABS-KEY (antibiotic* OR antimicrobial* OR antibacterial* OR penicillin* OR cephalosporin* OR aminoglycoside* OR quinolone* OR clindamycin OR metronidazole OR trimethoprim OR mupirocin OR "pseudomonic acid" OR neomycin OR "fusidic acid" OR framycetin) OR TITLE-ABS-KEY (polymyxin* OR chlortetracycline))) OR ((TITLE-ABS-KEY (antiseptic* OR soap* OR iodophor* OR povidone OR iodine OR chlorhexidine OR betadine OR alcohol* OR disinfectant* OR "hydrogen peroxide" OR "benzoyl peroxide" OR "gentian violet" OR hypochlorit*) OR TITLE-ABS-

KEY (eusol OR dakin* OR hexachlorophene OR benzalkonium OR "potassium permanganate" OR silver OR "silver sulphadiazine" OR honey*))))

Cochrane



#21	MeSH descriptor: [Mupirocin] explode all trees	MeSH	194
#22	MeSH descriptor: [Neomycin] explode all trees	MeSH	467
#23	MeSH descriptor: [Fusidic Acid] explode all trees	MeSH	95
#24	MeSH descriptor: [Framycetin] explode all trees	MeSH	31
#25	MeSH descriptor: [Polymyxins] explode all trees	MeSH	373
#26	MeSH descriptor: [Chlortetracycline] explode all trees	MeSH	17
#27	(antiseptic* or soap* or iodophor* or povidone or iodine or chlorhexidine or betadine or alcohol* or disinfectant* or hydrogen peroxide or benzoyl peroxide or gentian violet or hypochlorit* or eusol or dakin* or hexachlorophene or benzalkonium or potassium permanganate or silver or silver sulphadiazine or honey*)	Limits	39859
#28	MeSH descriptor: [Antisepsis] explode all trees	MeSH	110
#29	MeSH descriptor: [Soaps] explode all trees	MeSH	211
#30	MeSH descriptor: [Iodophors] explode all trees	MeSH	584
#31	MeSH descriptor: [Chlorhexidine] explode all trees	MeSH	1941
#32	MeSH descriptor: [Alcohols] explode all trees	MeSH	34946
#33	MeSH descriptor: [Benzoyl Peroxide] explode all trees	MeSH	282
#34	MeSH descriptor: [Gentian Violet] explode all trees	MeSH	36
#35	MeSH descriptor: [Hypochlorous Acid] explode all trees	MeSH	437
#36	MeSH descriptor: [Hexachlorophene] explode all trees	MeSH	30
#37	MeSH descriptor: [Silver] explode all trees	MeSH	194
#38	MeSH descriptor: [Silver Sulfadiazine] explode all trees	MeSH	160
#39	MeSH descriptor: [Honey] explode all trees	MeSH	143
#40	MeSH descriptor: [Anti-Infective Agents] explode all trees	MeSH	26985
#41	#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40	Limits	168900
#42	#5 and #41	Limits	145

Tables

Category	Author	Year	Study type	Sample Size	Number of infections (explanted)	Summary of results	Evidence level
P	Hirsch et al.	2007	Retrospective case series	95	3 (0)	Cefazolin as a single dose 30 min before skin incision. No major and 3 minor infections	4
P	Clark et al.	1980	Expert opinion	N/A	N/A	Authors described their own experience of various pre-operative, intraoperative and post-operative measures to reduce CI infection.	5
P	Basavaraj et al.	2004	Retrospective case series	292	12 (2)	Higher infection rate with C incision, extended endaural incision or long-term antibiotics	4
P	Almosnino et al.	2018	Case-control	188	0 (0)	No difference between single shot prophylaxis, controls or prolonged antibiotics prophylaxis.	3b
P	Garcia-Valdecasas et al.	2009	Cohort study	196	9 (9)	Surgical site risk infection rate was 8.1 times higher in patients treated only with ceftriaxone and classical postoperative prophylaxis compared to those also	2b

						given clarithromycin.	
P + M	Gluth et al.	2011	Expert opinion	n/a	N/A	Authors discuss their expert opinion on methods to prevent and manage cochlear implant infections including dealing with chronic otitis media first before implantation.	5
M	Kabelka et al.	2010	Retrospective case series	360	4 (2)	Pseudomonas spp. infections are difficult to treat and may require earlier explantation..	4
M	Davids et al.	2009	Retrospective case series	452	2 (2)	There were five major complications: two soft tissue infections, one extrusion, and two major seromas leading to device migration. Four of them involved loss of device fixation. Three required device explantation	4
M	Gawecki et al.	2016	Retrospective case series	1076	0 (0)	Revision surgery with resection of infected tissue, formation of a rotational two- layer flap preceded and supplemented by intensive targeted antibiotic therapy should be the first treatment option.	4
M	Low et al.	2013	Retrospective	432	8 (2)	Polyprolene and radiotherapy were quoted risk	4

			case series			factors for wound infections. Suggested management included 6 weeks of intravenous antibiotics, aggressive washouts and transposition of device if necessary.	
M	Olsen et al.	2018	Retrospective case series	653	11 (8)	The major and minor infection rates were 2% and 8%, respectively. The explantation rate due to infection was 1%. The most common pathogen found was Staphylococcus aureus and biofilm formation was found in 73% of the explantations.	4
M	Palau et al.	2012	Retrospective case series	350	11 (3)	In the surgical wound infection group the bacteria isolated were *Staphylococcus spp.* 6 out of 7 wound infections were successfully treated with oral antibiotics (co-amoxiclav and levofloxacin).	4
M	Rubinstein et al.	1999	retrospective case series	4	4 (0)	4 patients required surgery for infectious flap related issues where the implant was trans positioned and covered with pericranial with or without temporalis muscle flap.	4

M	Rubin et al.	2010	Expert opinion / policy statement	N/A	N/A	Authors describe their experience and evidence within the literature on how to manage various cochlear implantation complications.	5

Table 1. Summary of articles included in systematic review alongside level of evidence.

* *P = prevention, M = management,*